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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)
0975.1005-017

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on 4-21-2006

Signature Amy Comeau

Typed or printed name Amy Comeau

Application Number	Filed
10/043,432	01/10/2002

First Named Inventor
Junming Le

Art Unit	Examiner
1644	Phillip Gambel

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

Please see the attached Pre-Appeal Brief Conference Remarks.

I am the

☐ applicant/inventor.

☐ assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)

☒ attorney or agent of record.
Registration number 42,122

☐ attorney or agent acting under 37 CFR 1.34.
Registration number if acting under 37 CFR 1.34 _____

Deirdre E. Sanders
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April 21, 2006
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

☒ *Total of 1 forms are submitted.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Junming Le, Jan Vilcek, Peter Daddona, John Ghrayeb, David Knight and Scott Siegel		
Application No.:	10/043,432	Group:	1644
Filed:	January 10, 2002	Examiner:	Phillip Gambel
Confirmation No.:	3288		

For: METHODS OF TREATING CACHEXIA WITH CHIMERIC ANTI-TNF ANTIBODIES

CERTIFICATE OF MAILING OR TRANSMISSION
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PRE-APPEAL BRIEF CONFERENCE REMARKS

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Final Office Action mailed from the U.S. Patent and Trademark Office on November 21, 2005, Applicants respectfully request a pre-appeal brief conference. A Notice of Appeal is being filed concurrently with this request.

Background

On November 21, 2005, the Examiner issued a Final Office Action in the above-referenced application, rejecting pending claims under 35 U.S.C. § 112, first paragraph (written

description and enablement); 35 U.S.C. § 112, second paragraph (indefiniteness); 35 U.S.C. § 102(b); and 35 U.S.C. § 103. The Office Action also included obviousness-type double patenting rejections, which Applicants plan to overcome with terminal disclaimers. Applicants filed an Amendment After Final Rejection on March 14, 2006, to cancel Claims 3 and 16 and to place the remaining claims in condition for allowance. Because reference to cA2 was deleted in the claims, and information regarding deposit of the A2 antibody was provided, it is believed that the indefiniteness and enablement rejections will be overcome entirely. However, the Advisory Action dated April 11, 2006, indicates that the Amendment was not entered. In a telephone conversation on April 18, 2006, the Examiner indicated that the Amendment would be entered if the issues are not resolved after the pre-appeal brief conference.

Thus, the focus of these Remarks is on the remaining written description and prior art rejections, which relate to whether the claims reciting "TNFα-mediated cachexia associated with cancer" are supported in the specification and priority applications.

I. Applicants' Claims are Novel and Non-Obvious Because They are Entitled to Claim Priority Prior to Le *et al.* (WO 92/16553), which Published on October 1, 1992.

The pending claims are Claims 1-11 and 14-20. Claims 1-11, 14-15 and 17-20 were rejected under 35 U.S.C. § 102(b) for being anticipated by Le *et al.* (WO 92/16553), which is Applicants' PCT application (Reference AN4 of record). Claims 1 and 16 were rejected under 35 U.S.C. § 103(a) in view of Le *et al.* (WO 92/16553) and what was known and practiced at the time regarding pulmonary routes of administration. However, Le *et al.* (WO 92/16553), which was published on October 1, 1992, is not prior art because it was published after the priority date of the Applicants' claims. Further, WO 92/16553 is substantially identical to Applicants' priority application which was filed on the same day as WO 92/16553 was filed (March 18, 1992).

A. The Priority Date of Claims 1, 3-5, 11 and 14-20 is March 18, 1991

Claims 1, 3-5, 11 and 14-20 are entitled to claim the benefit of priority application USSN 07/670,827 (filed March 18, 1991). Claims 1, 3-5 and 11 recite "TNFα-mediated cachexia

associated with cancer." Claims 14-20 depend from these claims, and, therefore, contain the same limitation. This priority application teaches that the "[h]igh affinity chimeric anti-TNFα mAbs of the present invention, which have potent TNFα neutralizing activity, including TNFα-neutralizing fragments thereof, are useful as therapeutic agents for TNFα-mediated human disease...." (Page 10, lines 22-25 of the USSN 07/670,827 specification). It also discloses treatment of a number of TNFα-mediated diseases, including cancer, cachexia, neoplastic disease, and malignant disease involving TNFα-secreting tumors with the claimed antibodies. (See USSN 07/670,827, for example, at page 3, line 21 to page 5, line 23; page 10, line 22 to page 11, line 9; and page 39, line 20 to page 40, line 9).

The specification of this priority application also discloses that TNF was also known as "cachectin," that TNF is an important mediator of the cachexia in cancer. See USSN 07/670,827 at page 1, lines 15-16 and page 4, lines 11-14. In addition, it discloses that TNF is implicated in the pathogenesis of many diseases and disorders, including "neoplastic disease, e.g., in cachexia accompanying some malignancies...." USSN 07/670,827 at page 3, lines 21-26.

Further, it discloses that the association of TNF with cancer is often related to the host's catabolic state, and that a major problem in cancer patients is weight loss, usually associated with anorexia, which sometimes results in extensive wasting known as cachexia. See USSN 07/670,827 at page 4, lines 1-15.

With regard to treatment of TNFα-mediated cachexia associated with cancer, the Examiner acknowledges that the mechanism of treatment would be the same or nearly the same regardless of the TNFα-mediated disease or condition. (Page 2, November 21, 2005 Office Action).

Thus, the priority application USSN 07/670,827 (filed March 18, 1991) discloses treatment of TNFα-mediated disease, including TNFα-mediated cachexia and cachexia associated with cancer, with the claimed antibodies, in sufficient detail such that one of ordinary skill in the art can reasonably conclude that Applicants were in possession of the claimed invention, and Applicants are entitled to claim the benefit of it. This priority application has been properly referenced on page 1 of the specification in compliance with 35 U.S.C. § 120.

B. The Priority Date of Claims 2 and 6-10 is at Least as Early as March 18, 1992

Claims 2 and 6 recite epitopes of TNF, and are entitled to claim the benefit of priority application USSN 07/853,606 (filed March 18, 1992), which provides sufficient written description and enablement for these claims. See, for example, the specification at page 7, lines 29-35; page 8, lines 18-23; page 12, lines 4-14; page 13, lines 8-18; page 20, lines 19-33; Figures 13 and 15; and Example XIII, particularly pages 68 and 69). Claims 7-10 recite antibody sequences, and are also entitled to claim the benefit of this priority application, which provides sufficient written description and enablement for these claims (see, for example, the specification at page 12, lines 20-23; Figures 17A-B; and page 24, lines 5-17). Please note that the SEQ ID NO. identifiers were later amended to correct an inadvertent error in the specification to clarify that Figure 17B (renumbered Figure 16B after amendment), is a nucleic acid sequence (SEQ ID NO.: 4) and corresponding amino acid sequence (SEQ ID NO.: 5) of the heavy chain variable region of the cA2 monoclonal antibody (see, for example, page 2 of the Amendment filed in US Serial No.: 08/324,799 on March 14, 1997, as discussed in detail). The nucleic acid sequence (SEQ ID NO: 2) and corresponding amino acid sequence (SEQ ID NO:3) of the light chain variable region are also disclosed in this specification. This priority application has been properly referenced on page 1 of the specification in compliance with 35 U.S.C. § 120.

II. Claims 1-11 and 14-20 Satisfy Written Description Requirements Under 35 U.S.C. § 112, first paragraph

Claims 1-11 and 14-20 satisfy the written description guidelines under 35 U.S.C. §112, first paragraph. The instant specification teaches that the antibodies of the present invention neutralize and inhibit TNFα *in vivo* and are useful for treating TNFα-mediated disease. See the specification, for example at page 16, lines 9-26 and page 57, line 17 to page 59, line 14. The specification also discloses treatment of a number of TNFα-mediated diseases, including cancer, cachexia and malignant disease involving TNFα-secreting tumors with the claimed antibodies. (See, for example, the specification, for example at page 3, lines 1-13; page 16, lines 9-26; and page 57, line 17 to page 59, line 14).

The specification also discloses that TNF is implicated in the pathogenesis of many diseases and disorders, including neoplastic disease and cachexia associated with cancer. (See, for example, the specification, for example at page 3, lines 1-13).

It discloses that the association of TNF with cancer is often related to the host's catabolic state, and that a major problem in cancer patients is weight loss, usually associated with anorexia. It further discloses that the extensive wasting which is associated with cancer is known as "cachexia," and that cachexia includes anorexia. See the specification, for example, at page 3, lines 1-13. With regard to treatment of TNFα-mediated cachexia associated with cancer, the Examiner acknowledges that the mechanism of treatment would be the same or nearly the same regardless of the TNFα-mediated disease or condition. (Page 2, November 21, 2005 Office Action).

Thus, the specification discloses treatment of TNFα-mediated disease, including TNFα-mediated cachexia and cachexia associated with cancer, with the claimed antibodies, in sufficient detail such that one of ordinary skill in the art can reasonably conclude that Applicants were in possession of the claimed invention.

CONCLUSION

In view of the above remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue.

Respectfully submitted,
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